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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,276	09/19/2005	Danilo Giribone	18614 (PCT27405A)	3819
23389 7590 02/07/2008 SCULLY SCOTT MURPHY & PRESSER, PC 400 GARDEN CITY PLAZA SUITE 300 GARDEN CITY, NY 11530			EXAMINER KOSACK, JOSEPH R	
			ART UNIT	PAPER NUMBER
			1626	
			MAIL DATE	DELIVERY MODE
			02/07/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/523,276	<b>Applicant(s)</b> GIRIBONE ET AL.	
	<b>Examiner</b> Joseph Kosack	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-6 are pending in the instant application.

#### ***Amendments***

The amendment filed on December 6, 2007 has been acknowledged and has been entered into the application file.

#### ***Previous Claim Rejections - 35 USC § 112***

Claim 7 provided for the use of compounds of Formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. The claim has been cancelled, and the rejection is withdrawn.

#### ***Previous Claim Rejections - 35 USC § 101***

Claim 7 was previously rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. The claim has been cancelled, and the rejection is withdrawn.

#### ***Previous Claim Rejections - 35 USC § 102***

Claims 1-4 were previously rejected under 35 U.S.C. 102(b) as anticipated by Tang et al. (USPN 5,834,504).

Applicant has traversed the rejection on the grounds that the reference does not teach compounds of a high degree of radiochemical purity and that the natural abundance of carbon does not include  $^{14}\text{C}$ .

The Examiner respectfully disagrees. The claim is not drawn to a compound "of a high degree of radiochemical purity," but is drawn to a compound in which one carbon atom is a  $^{14}\text{C}$ . Claims are given their broadest reasonable interpretation while in front of the U.S. Patent and Trademark Office, that being that a reference that teaches any concentration of the claimed compound would be anticipatory and would render the claim rejected under 35 U.S.C. 102. Additionally, the Argonne National Laboratory reported in 2005 that  $^{14}\text{C}$  is present in the natural abundance, even if it is an extremely small fraction (about two trillionths). Therefore, each and every limitation of the claims have been met, and the rejection is valid and maintained.

***Previous Claim Rejections - 35 USC § 103***

Claims 1-5 and 7 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (USPN 5,834,504) in view of Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

Applicant has traversed the rejection on the grounds that there are several differences between the compounds and the process of making such compounds in Tang et al. and that of the present of invention, and that the secondary reference has a different utility than the base reference.

This is not found to be persuasive because the Applicant did not point out what the supposed differences between Tang et al. and the instant claims are. Also that Plieninger et al. was used to supplement the isotopically labeled carbon atom of the instant claims, and even though Plieninger et al. is drawn to a different utility than that of Tang et al., one of skill in the art would look to Plieninger et al. through a structure

search to get the building block to isotopically label the compound of Tang et al.

Additionally, as stated above, the claim is not drawn to a compound "of a high degree of radiochemical purity," but is drawn to a compound in which one carbon atom is a  $^{14}\text{C}$ .

The rejection is maintained except for claim 7 which has been cancelled.

Claim 6 was previously rejected under 35 U.S.C. 103(a) as being unpatentable over Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

Applicant has traversed the rejection on the grounds that the compounds of claim 6 are not disclosed or suggested by Plieninger et al. and that there is no motivation to modify the prior art compounds with a reasonable expectation of success.

The rejection is maintained because Applicant has not pointed out specifically what flaws the *prima facie* case has and because a motivation and reasonable expectation of success was provided by the Examiner in the previous action.

#### ***Claim Rejections - 35 USC § 102***

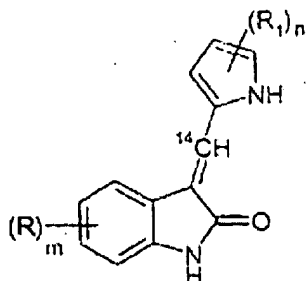
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 rejected under 35 U.S.C. 102(b) as anticipated by Tang et al. (USPN 5,834,504).

The instant application is drawn to compounds of formula I:



with substitutions as defined as well as a method of making by reacting an optionally substituted pyrrolinecarboxaldehyde with an oxindole in basic conditions. Included is the species 3-[(3,5-dimethyl-1H-pyrrol-2-yl)[<sup>14</sup>C]methylene-1,3-dihydro-2H-indol-2-one.

Tang et al. teach the compound 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene-1,3-dihydro-2H-indol-2-one along with the method of making by reacting the oxindole with optionally substituted pyrrolinecarboxaldehyde in piperidine. This reads on the claims because <sup>14</sup>C is within the natural abundance of carbon atoms and therefore the compound is inherently present in Tang et al.'s synthesis. See column 22, lines 42-49.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title; if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

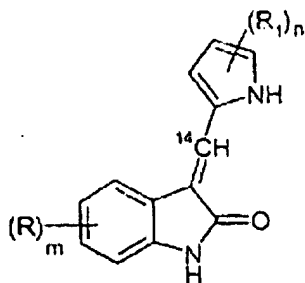
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 7 rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (USPN 5,834,504) in view of Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

The instant application is drawn to compounds of formula I:



with substitutions as defined and a method of making by reacting an optionally substituted pyrrolinecarboxaldehyde with an oxindole in basic

conditions, specifically pyrrolidine. Included is the species 3-[(3,5-dimethyl-1H-pyrrol-2-yl)[<sup>14</sup>C]methylene-1,3-dihydro-2H-indol-2-one.

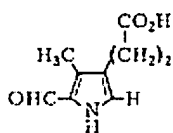
Determination of the scope and content of the prior art (MPEP §2141.01)

Tang et al. teach the compound 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene-1,3-dihydro-2H-indol-2-one along with the method of making by reacting the oxindole with optionally substituted pyrrolinecarboxaldehyde in piperidine. See column 22, lines 42-49.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Tang et al. do not teach that <sup>14</sup>C is present in the methylene group in more than the natural abundance, nor that the synthesis is done in pyrrolidine.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)



Plieninger et al. teach in which the carbon of the aldehyde group is <sup>14</sup>C. See page 196, compound 5 and page 198, second full paragraph. One of skill in the art would be able to make the switch from piperidine to pyrrolidine as the base for reaction as they are both cyclic nitrogenous bases. Additionally, one of skill in the art routinely uses radioisotopes for studies within the body for absorption, distribution, metabolism, and excretion studies.

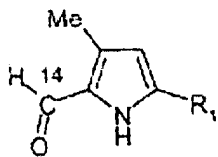
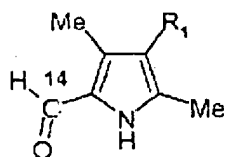
Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to follow the synthetic scheme of Tang et al. with the <sup>14</sup>C replacement of Plieninger et al. using pyrrolidine instead of piperidine to

make the claimed invention with a reasonable expectation of success. The motivation to do so is that radiolabeled compounds can be easily analyzed by mass spectroscopy in order to determine various aspects of the body, such as how much unnatural testosterone is within a human's system.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

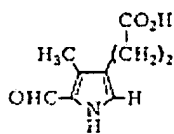
Claim 6 rejected under 35 U.S.C. 103(a) as being unpatentable over Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

The instant application is drawn to compounds of the formulae



with substitutions as defined.

Determination of the scope and content of the prior art (MPEP §2141.01)



Plieninger et al. teach

in which the carbon of the aldehyde group is

<sup>14</sup>C. See page 196, compound 5 and page 198, second full paragraph.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Plieninger et al. do not teach a methyl group in the 5-position of the pyrrolidine.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

It is known that compounds having similar structures have similar effects, especially when the difference is a hydrogen over a methyl group, which also provides

the motivation and the reasonable expectation of success. See the decision of In re Wood, Whittaker, Stirling, and Ohta (199 USPQ 137).

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

### **Conclusion**

Claims 1-6 are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

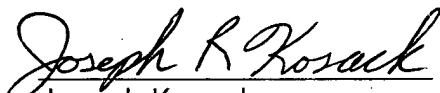
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-Th 6:30 A.M. until 5:00 P.M.

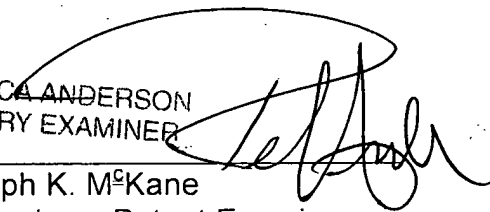
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Joseph Kosack  
Patent Examiner  
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REBECCA ANDERSON  
PRIMARY EXAMINER

Joseph K. McKane  
Supervisory Patent Examiner  
Art Unit 1626